Applicants' specification, for example, at page 3, lines 16-27. New claim 27 is supported by Applicants' specification, for example, at page 4, lines 19-22. New claim 28 is supported by Applicants' specification, for example, at page 4, lines 29-31. No new matter is introduced by the amendments to claim 1 and 14 or by introduction of new claims 21-28.

Restriction/Election Requirement

The Examiner maintained the restriction with respect to Group I and Group II in view of the traversal by Applicants. Applicants have canceled claims 12 and 13 without prejudice. All of the pending claims are in Group I.

Drawing

The Examiner objected to the drawings because no detail was discernable in the photocopies of the drawing submitted for examination. The Examiner further noted that photographs only are acceptable for examination purposes unless a petition is granted permitting their filing as formal drawings. Applicants are preparing formal drawing for submission. The formal drawings will be submitted in the near future along with a petition to accept photographs. Cells are visible in the photograph images. If the Examiner requires photographs for examination purposes prior to receipt of the formal drawing, the Examiner is requested to telephone Applicants' undersigned representative.

Rejections Over Bayne alone

The Examiner rejected claims 1-5 and 9-11 under 35 U.S.C. §102(b) as being anticipated by or, in the alternative, under 35 U.S.C. §103(a) as obvious over EP 0476983 to Bayne et al. (the EP Bayne application). The Examiner cited the EP Bayne application for disclosing fixed umbilical veins coated with proteins and growth factors. Applicants believe that the EP Bayne application only discloses the use of growth factors to stimulate cell cultures of endothelial cells and the association of growth factors with synthetic polymer blood vessels. Applicants respectfully request

reconsideration of the rejections over Bayne alone in view of the following comments.

The primary focus of the EP Bayne application is on the isolation and characterization of vascular endothelial cell growth factor II (VEGF II) from mammalian glioma cells. The examples in the EP Bayne application focus on the isolation and characterization of the growth factor. The EP Bayne patent further describes the use of VEGF II "in the promotion of tissue repair." This discussion is found mainly on page 8 of the EP Bayne application. The EP Bayne application discusses the use of VEGF II to stimulate vascular endothelial cells in cell culture. This is described on page 8, lines 8-17 and 27-29. The cells are then plated onto synthetic polymer substrates for the formation of an artificial blood vessel, see page 8, lines 17-19 and 30-35.

The EP Bayne application further describes the coating of VEGF II onto a synthetic polymer support prior to implantation of the artificial blood vessel into the patient, page 8, lines 20-21. Following implantation, it is speculated that endothelial cells will colonize the artificial surface. See page 8, lines 20-21. The EP Bayne application does not teach or suggest associating VEGF with any type of tissue, as described and claimed by Applicants. While the EP Bayne application discloses the administration of VEGF II as a drug to a patient for repair of the native tissue, see page 8, lines 36-43, the EP Bayne application does not describe association of VEGF with tissue, such as allograft or xenograft tissue. Applicants have demonstrated the successful colonization of tissue by endothelial cells following association of VEGF with the tissue.

Since the EP Bayne application does not teach or suggest tissue, such as allograft or xenograft tissue, the EP Bayne application does not anticipate or render obvious Applicants' claimed invention. Applicants respectfully request the withdrawal of the rejection of claims 1-5 and 9-11 under 35 U.S.C. §102(b) as

being anticipated by or, in the alternative, under 35 U.S.C. §103(a) as obvious over the EP Bayne application.

Rejections Over Tischer and Orton

The Examiner rejected claims 1, 2, 6, 7, 9-11 and 14-15 under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent 5,194,596 to Tischer et al. (the Tischer patent) in view of U.S. Patent 5,192,312 to Orton (the Orton patent). In particular, the Examiner cited the Tischer patent for disclosing soaking a transplant with VEGF prior to implantation. The Examiner cited the Orton patent for disclosing allograft and xenograft tissues for use in forming growth factor treated tissue. Applicants have amended claim 1 to more distinctly claim their invention. Applicants respectfully request reconsideration of the rejections over Tischer and Orton in view of the following comments.

The Tischer patent focuses on the isolation and characterization of two particular recombinant vascular endothelial growth factors. The Tischer patent includes a discussion of the uses of VEGF from column 10, line 63 to column 12, line 55. Most of the discussion focuses on the use of VEGF as a drug that is applied topically or intravenously. A paragraph from column 11, line 65 to column 12, line 19 of the Tischer patent describes the use of VEGF in vascular graft surgery. In particular, the Tischer patent discloses the application of VEGF to the surface of a graft using a "thickened carrier material," such as a 1-5% carbopol composition. Note that carbopol is a vinyl polymer. A copy of the relevant Merck Index listing is enclosed.

The Tischer patent does not describe association of VEGF with a tissue substrate by direct attachment, association with an adhesive or by chemical binding. Applicants' claim 1 has been amended to indicate that the growth factor is associated with the tissue by association with an adhesive or chemical binding. Applicants' claim 14 has been amended to indicate that the growth

factor is associated with the tissue by direct attachment, association with an adhesive, or chemical binding.

The Orton patent discloses the association of growth factors, such as fibroblast growth factor, with tissue by soaking the tissue in a solution containing the growth factor. The Orton patent does not disclose association of a growth factor with tissue using an adhesive or by chemical binding. Also, the Orton patent does not teach or suggest VEGF.

Since neither the Tischer patent nor the Orton patent disclose association of a growth factor with tissue using an adhesive or by chemical binding, the combined teachings of the Tischer patent and the Orton patent do not render Applicants' claim 1, as amended, obvious. Claims 2, 6, 7 and 9-11 depend from claim 1 and are not obvious for the same reasons as claim 1. Furthermore, since neither the Tischer patent or the Orton patent disclose association of VEGF for the formation of a heart valve prosthesis, the combined teachings of the Tischer patent and the Orton patent do not render claims 14 or 15 obvious. Applicants respectfully request the withdrawal of the rejection of claims 1, 2, 6, 7, 9-11 and 14-15 under 35 U.S.C. §103(a) as being unpatentable over the Tischer patent in view of the Orton patent.

Rejection of Claim 8 Over Tischer, Orton and Carpentier

The Examiner rejected claim 8 under 35 U.S.C. §103(a) as being unpatentable over the Tischer patent and the Orton patent as applied to claim 1, and further in view of U.S. Patent 4,648,881 to Carpentier et al. (the Carpentier patent). The Examiner noted that the Tischer patent and the Orton patent failed to disclose pericardial tissue. The Examiner cited the Carpentier patent for disclosing bovine pericardial tissue for constructing heart valves. Applicants respectfully request reconsideration of the rejection of claim 8 based on the following discussion.

The deficiencies of the Tischer patent and the Orton patent with respect to Applicants' claimed invention were noted above.

Claim 8 depends from claim 1 and would be free of the teachings of the Tischer patent and the Orton patent for the same reasons as claim 1. The Carpentier patent does not teach or suggest the use of growth factors. Therefore, the Carpentier patent does not make up for the deficiencies of the Tischer and Orton patents. Since the combined teachings of the Tischer patent, the Orton patent and the Carpentier patent do not teach or suggest association of a growth factor with tissue using an adhesive or by chemical binding, the patents do not render claim 8 obvious. Applicants respectfully request the withdrawal of the rejection of claim 8 under 35 U.S.C. §103(a) as being unpatentable over the Tischer patent and the Orton patent as applied to claim 1, and further in view of the Carpentier patent.

CONCLUSIONS

In view of the foregoing amendments and remarks, Applicants submit that the application is in condition for allowance, and such action is respectfully requested. The Examiner is invited to telephone the undersigned attorney to discuss any questions or comments that the Examiner may have.

The Commissioner is authorized to charge any fee deficiency required by this paper or credit any overpayment to Deposit Account No. 23-1123.

Respectfully submitted,

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